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Does BCG (Bacillus of Calmette and Guerin) vaccination of new born babies rapidly reduce their blood level of iron by increasing levels of the hormone hepcidin?

Submission date
25/07/2013

Recruitment status
No longer recruiting

Registration date
03/09/2013

Overall study status
Completed

Last Edited
18/12/2017

Condition category
Neonatal Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Bacillus-Calmette Guerin (BCG) vaccination is given to babies at birth to protect them against tuberculosis (TB). There is some evidence that this vaccination might also protect infants against other infections, but it is not known how this might happen. Our aim is to find out whether BCG vaccination might decrease iron levels in the blood stream. As iron is very important for the growth of many infectious diseases, such a reduction might limit the growth of these organisms. This might therefore provide babies with protection against many serious diseases. This study is a small initial study to compare the levels of iron and its controlling hormone in BCG vaccinated and unvaccinated babies in the first few days of life. The results of this study will be used to design future research.

Who can participate?
Any healthy baby born and registered in the study area (West Kiang, The Gambia) is free to participate. They can only be included in the study if they are seen within the first 24 hours of life and consent is gained from the mother.

What does the study involve?
Babies participating in the study will be randomly assigned to receive BCG vaccination either on the first day of life or delayed to 24-96 hours of age. All infants will have two blood tests taken, one immediately after birth (before any vaccinations are given) and a second at either 24 or 72 hours after the first blood test. Any child receiving delayed BCG vaccination will then be vaccinated following their second blood test. All infants will receive all other routine vaccinations as normal at birth. A medical professional will clinically review all infants at the time of their blood tests. Any child deemed to be unwell will be referred to the research clinic for treatment. Each infants study involvement will be complete by 4 days of age. The blood samples taken from each infant will be tested for markers of iron status, as well as for levels of the hormone regulating iron status.

What are the possible benefits and risks of participating?
Participants benefit from early review by trained medical professionals in their homes. Any unwell child will be transferred directly to receive medical attention free of charge. Participants also benefit by receiving vaccinations earlier than they otherwise would. There is a very small increased risk of tuberculosis infection in infants who have delayed BCG vaccination compared to those that receive it on the first day of life. This is minimised by excluding infants born into families with a known case of active TB. The very short delay in vaccination also makes the risk of infection minimal. The taking of two blood samples from participants is likely to cause a small amount of discomfort. This will be minimised by comfort measures such as breast-feeding. Blood sampling also poses a potential risk of introducing infection to the baby. This will be minimised by making sure all procedures are carried out in a sterile way. The volume of blood taken at each of the blood tests is well within recommended guidelines and should not pose any risk to infants.

Where is the study run from?
This study is run from the MRC-Keneba field station in The Gambia.

When is the study starting and how long is it expected to run for?
The study started in June 2013 and is expected to last for 6 months. It will continue until 80 infants (40 male and 40 female) have been recruited.

Who is funding the study?
The study is funded by the Medical Research Council, UK.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
SCC 1325v2

Study information

Scientific Title
Does neonatal BCG (Bacillus of Calmette and Guerin) vaccination elicit an acute hepcidin-mediated Hypoferremia: a pilot randomised controlled trial

Acronym
BCG-Hypo

Study objectives
We hypothesise that the inflammation stimulated by BCG vaccination of neonates causes a reduction in serum iron by enhancing the IL-6 (interleukin-6) driven production of hepcidin. We further hypothesise that this reduction of serum iron produces protection against heterologous pathogens (though this will not be tested in this pilot study).The null hypothesis is that there will be no difference in serum iron status and the inflammatory-iron axis at 24 hours and 72 hours of age between BCG vaccinated and unvaccinated individuals.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Joint Gambia Government/MRC Unit The Gambia Ethics Committee
2. The London School of Hygiene and Tropical Medicine Ethics Committee

Study design
Pilot un-blinded randomised controlled trial

Primary study design
Interventional

Study type(s)
Screening

Health condition(s) or problem(s) studied
The effect of BCG vaccination on serum iron status in neonates

Interventions
BCG-Danish 0.05ml Intra-dermally. Subjects randomised to receive BCG vaccination on the first day of life (<24 hours of age) or delayed to following their second blood test (24-96 hours of age). Follow-up is until 4 days of age. Children are clinically assessed by a paediatrician/nurse at each blood sample visit during this time (twice). There is no current longer term follow-up.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)

1. Plasma transferrin saturation
2. Plasma hepcidin level: ELISA - Bachem-25
3. Plasma IL-6 level: ELISA

All outcomes will be measured at baseline (cord blood), <24 hours of age and at either 24 (+/- 4 hours) or 72 hours (+/- 4 hours) from the time of the first venous blood sample. The timing of the second sample (24 or 72 hours) is randomly assigned.

Key secondary outcome(s))
1. Serum iron
2. Serum Unbound Iron Binding Capacity
3. Ferritin
4. Transferrin
5. Red cell parameters (haemoglobin, mean corpuscular volume, mean corpuscular haemoglobin, mean corpuscle haemoglobin concentration, haematocrit, red cell distribution width, red blood cell count) measured by Automated Analyser (Medonic)
Iron parameters are measured by Automated Cobas Analyser (Roche).

Completion date
17/12/2013

Eligibility

Key inclusion criteria
1. Neonates seen within the first 24 hours of age
2. Neonates resident in West Kiang, The Gambia and enrolled in the West Kiang Demographic Surveillance System

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Neonate

Sex
All

Key exclusion criteria
1. Neonates with birth weight less than 2000g
2. Neonates with severe birth asphyxia
3. Neonates with major congenital malformations
4. Neonates born to mothers with known HIV or active tuberculosis
5. Neonates born into families with a known active case of tuberculosis in the same compound
6. Neonates currently enrolled in another research study.

Date of first enrolment
17/06/2013

Date of final enrolment
17/12/2013

Locations

Countries of recruitment
United Kingdom

England

Gambia

Study participating centre
London School of Hygiene and Tropical Medicine
London
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Sponsor information

Organisation
Medical Research Council (UK)

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC), UK. Grant number: MC-A760-5QX00

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	12/06/2015		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes